REMARKS

Claims 1-3, 9, 10 and 18-45 have been cancelled. New claims 46-52 have been added. New claims 46-52 are supported by cancelled claims 1 and 32, and by the Specification, at least at page 6, lines 11-23; at page 7, lines 7-32; and at page 8, lines 3-7 and 18-23. New claims 46-52 are directed to a method, and are consistent with elected Group I.

Claims 4-8, 11-14 and 16 have been amended to make them dependent on, and consistent with, new independent claim 46. No new matter has been added. Claims 4-8, 11-17 and 46-52 are present in the application.

Interview Summary

Applicants would like to thank Examiner Song for the helpful discussion with Applicants' representative on November 2, 2006. During this discussion, the references of record were reviewed with respect to the language of independent claim 1.

Request for Reconsideration

Obtaining high-quality protein crystals is typically challenging. No known methods exist to *a priori* predict crystal-producing solution conditions, leaving high throughput screening as the only option. Current crystallization screening platforms have limited capabilities. The equilibrium state reached during a screening experiment does not guarantee the occurrence of a phase transition (formation of a gel, liquid-liquid separation, aggregates, crystals, a film, or combinations thereof; also referred to as a "hit"). In addition, crystals are not typically produced once equilibrium is reached, leaving no definitive end point in the experiment. Typical experiments can take from weeks to months for a phase transition to be observed. Screening methods provide, per experiment, binary information (hit or no-hit) at best and often have a low success rate (typically < 20%), requiring a large number of experiments to be performed to find a few suitable crystallization conditions.

The claimed invention can overcome limitations of current crystallization platforms. New independent claim 46 is directed to a method of determining crystal growth conditions that includes placing a first plurality of solutions of a compound in a first plurality of chambers, to provide a first plurality of systems; and removing solvent from the first plurality of solutions, to form a solid in each chamber; where the solid of a system of the first plurality includes a crystal. Each solution of the first plurality has a concentration of the compound, and each chamber of the first plurality includes an evaporation member having an effective A/L. One of the concentration or the effective A/L is substantially the same for the first plurality of systems, and the other of the concentration or the effective A/L is different for the first plurality of systems.

The method of new independent claim 46 further includes placing a second plurality of solutions of the compound in a second plurality of chambers, to form a second plurality of systems; and removing solvent from the second plurality of solutions, to form a solid in each chamber; where the solid of a system of the second plurality includes a crystal having a highest quality relative to the solids of the other systems of the second plurality. Each solution of the second plurality has a concentration of the compound, and each chamber of the second plurality includes an evaporation member having an effective A/L. The concentration or the effective A/L that was different for the first plurality of systems, and that was associated with the system of the first plurality having the solid that included the crystal, is substantially the same for the second plurality of systems. The concentration or the effective A/L that was substantially the same for the first plurality of systems is different for the second plurality of systems.

The term "effective A/L" is described in the Specification as an evaporation member property that is proportional to the rate of evaporation of solvent from a solution in a chamber that includes the evaporation member (page 6, lines 11-15). The effective A/L of an evaporation member can be determined experimentally by the test provided in the Specification (page 6, lines 15-19).

Rejection under 35 U.S.C. § 103

The rejection of the claims as obvious under 35 U.S.C. § 103(a) over U.S. Patent No. 6,406,903 B2 to Bray *et al.* (Bray) in view of Shu, Z-Y *et al.*, *J. Crystal Growth* 192 (1998) 282-289 (Shu) has been obviated by appropriate amendment. Independent claims 1 and 32 have been cancelled and replaced with new independent claim 46. The method of claim 46 includes removing solvent from solutions of first and second pluralities of systems to form a solid in each system, where one plurality of systems includes different solution concentrations but substantially the same effective A/L values, and the other plurality of systems includes different effective A/L values but substantially the same solution concentrations. Claim 46 also includes setting a value of one of the concentration or the effective A/L to be substantially the same for the second plurality of systems, where this value was different for the first plurality of systems and was associated with a system that yielded a crystal. These aspects of the claimed method are not disclosed or suggested in the references.

Bray discloses a system for dynamically controlling the growth of crystals from solutions by separately controlling the nucleation environment and the crystal growth environment (col. 3, lines 21-25; col. 4, lines 31-65). Initial solution concentrations are fixed for all experiments, based on pre-mixed stock solutions (col. 8, lines 6-27). A first set of crystal growth parameters is used prior to nucleation, and a second set of parameters is used after nucleation has been detected (col. 10, lines 19-22). Crystal growth parameters that can be varied include the rate of evaporation and the temperature (col. 16, lines 29-51). Bray discloses non-dynamic experiments in which evaporation rates were varied between different crystallizations, and where the crystallization solutions had identical concentrations (col. 8, lines 33-46; Figures 9 and 10). These experiments demonstrated general trends between evaporation rates and crystal sizes (col. 8, lines 38-46). The trends were used for subsequent dynamic crystallizations in which evaporation rates varied during the course of crystallization, and where the crystallization solutions again had identical concentrations (col. 8, lines 46-60).

Shu discloses a system for dynamically controlling the growth of crystals from solutions in real time (p. 283, right column, 2nd paragraph, 1st sentence). The progress of evaporation of a solution is monitored by continuously measuring the mass of the solution (p. 283, right column, 2nd paragraph, 2nd sentence). When the mass of the solution decreases to a value corresponding to the known nucleation concentration, the salt concentration of a reservoir near the solution is changed, causing a decrease in the rate of evaporation (p. 286, left column, 2nd paragraph through p. 287, left column, 2nd paragraph). Control crystallizations were also performed, in which the evaporation rate was not dynamically controlled but was allowed to vary during the course of crystallization (Tables 1 and 2, on pages 285 and 287). When different lysozyme concentrations of 16 mg/mL and 25 mg/mL were investigated using the dynamic method, the crystallization results were similar (p. 286, right column, 2nd paragraph). Neither of these concentrations was used for subsequent crystallization experiments.

Bray and Shu do not disclose or suggest removing solvent from solutions of first and second pluralities of systems, where one of the pluralities includes different solution concentrations but substantially the same effective A/L values. In the dynamic methods of the references, the rates of evaporation change during the course of crystallization, such that the dynamic systems cannot have a parameter related to the rate of evaporation that is substantially the same for a plurality of crystallizations. In the non-dynamic methods of the references, either the evaporation rates are varied between different crystallizations (Bray) or the evaporation rates change during the course of crystallization (Shu). Thus, there is no teaching or suggestion in the references to set a parameter related to the rate of evaporation to be substantially the same for a plurality of crystallizations.

The references also do not disclose or suggest setting a value of one of the concentration or the effective A/L to be substantially the same for the second plurality of systems, where this value was different for the first plurality of systems and was associated with a system that yielded a crystal. Bray changes crystallization parameters dynamically, based on the detection of nucleation or

aggregation. Shu also changes crystallization parameters dynamically, but based on the progress of evaporation. Neither reference sets a parameter to be substantially the same for a set of crystallizations, based on the results of a previous set of crystallizations in which that parameter was varied.

Bray and Shu, alone or in combination, do not disclose or suggest each and every element of the claims. Accordingly, the references cannot anticipate or make obvious the pending claims, and Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

All of the grounds raised in the present Office Action for rejecting the application are believed to be overcome or rendered moot based on the remarks above. Thus, it is respectfully submitted that all of the presently presented claims are in form for allowance, and such action is requested. Should the Examiner feel a discussion would expedite the prosecution of this application, the Examiner is kindly invited to contact the undersigned at (312) 876-1400.

Respectfully submitted,

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